Stratified Medicine in Psychiatry: What Service Users, Carers and the Public Think

Introduction

Stratified medicine has been described as the 'next big thing' in medical research, with millions of pounds in funding from government bodies like the Medical Research Council and Technology Strategy Board, and charities like Cancer Research UK. At heart, it's a simple idea; it means treating conditions based on tests which determine the likely treatment response, both its success and the side effects. These tests might be genetic (as in modern cancer treatment) involve imaging studies (as proposed in psychiatry) or be based on blood tests for biomarkers.

There are two reasons stratified medicine may be important in psychiatry and more specifically for the treatment of people diagnosed with psychosis. First, antipsychotic medication currently is very much a matter of trial and error. Several medicines may be tried before an appropriate one is found and some service users never receive adequate treatment. What's more, these medications frequently provoke unwanted effects which some service users can experience as worse than the diagnosed illness. Secondly, all anti-psychotics currently available target one neurochemical system – the dopamine system. But researchers and clinicians now hypothesise that for some people with a diagnosis of psychosis dopamine pathways are not disturbed and a different neurochemical system, the glutamate pathway, is implicated. If this were so, it would explain why dopaminergic drugs do not work for everyone and would open the possibility of developing medications which specifically target the glutamate system. For this to be successful we need to develop a method to tell which patients are in each group.

While this might sound like a simple case of research improving medical outcomes there are inevitable wrinkles. The research which aims to identify the markers of likely treatment response will involve medical data sharing on a massive scale, with serious questions being asked about the readiness of the UK healthcare system to manage data securely and ethically. Once techniques are developed there will be inevitable changes to the experience of individual patients. To introduce stratified medicine in psychiatry will mean that patients and service users will need to undergo tests to identify biomedical markers which indicate which drug they should take. Some of these tests are quite simple – for example, needle aspirations or check swabs – but others are much more invasive – for example, various forms of body or brain imaging which in turn can involve intravenous drips and chemical contrast agents and last several hours. It is important to find out how far patients and service users are willing to go to find a biomarker that could indicate which medication is appropriate for them. Further issues concern confidentiality and, in terms specifically of genetic tests, the possibility of data sharing. Finally, not all psychiatric service users believe that their problems are of biomedical origin; an assumption which underlies investment in this type of research.

Two recent research projects have explored these issues with the public, service users and carers. The Service User Research Enterprise (SURE) at King's College London aims to put the service user voice at the heart of mental health research. As preparation for clinical work

on the dopamine and glutamate system, SURE was asked to investigate patient, service user and carer views. Three service user focus groups were held in Manchester, London and Edinburgh (totalling 18 people) and one carer focus group in London, at which there were eight participants. Each group discussed current approaches to prescribing antipsychotic medication and views of stratified medicine as an alternative, and explored participants' attitudes towards particular test types and willingness to join a hypothetical clinical trial.

Concurrently, the Technology Strategy Board, one of the main funders of stratified medicine research in the UK, commissioned research consultancy OPM Group to carry out a dialogue programme with the public, patients and stakeholders to understand how they interpreted these potential shifts in the way healthcare is delivered. Over 6 months OPM involved around 180 people in deliberative workshops where they learnt about and debated the potential of stratified medicine.

Findings

Current practice and the potential for stratified medicine

The principle advantage of a stratified approach to treatment is that it eliminates the need to try one treatment after another to find one that works. For both the public and psychiatric service users the value of this was recognised, although with different degrees of emphasis. The public saw an opportunity for more efficient treatment; less inconvenient trips to the GP for different rounds of treatment; an end to waiting months between each hospital appointment. For service users and their carers the same principle applied to a greater degree:

> What got me was all the mucking about with the different antipsychotics, d'you know what I mean? I mean it took them a long time.... about ten years to find the right one for me?... Ten years to find, to put me on that **(Service User)**

> With my daughter it took seven years of trying different medication... it has taken a long time. It's been, she's been under psychiatric care for at least sixteen years **(Carer)**

The prevalence of side effects was another motivator for public participants with experience of ill health to support stratified approaches; they commonly reported complex patterns of symptoms, side effects and co-morbidities. Some participants with a chronic physical condition described how the side effects could sometimes be as bad as the illness itself. Similarly among services users most participants expressed negative views on their experiences with medication. Discussions were dense with talk of never finding a drug without very debilitating side effects.

It seems that all the drugs seem to be hit and miss. None of them seem to work. In fact I find my son tends to take the drug and then after a while he gets immune to it and then the old symptoms come back… and the drugs completely knock him out. …any other sort of medication if you used the same sort of drug effects, people would be horrified.

(Carer)

Some people eventually found a helpful medication but the experience left others with the view that medication in general was to be avoided. These participants were sometimes cynical about the positive effects of medication in general, believing that they were not measurable and were outweighed by side effects:

I mentioned about the negative side effects. I would like them to be explained to me - what sort of positive effects I could expect from this treatment and what I should be looking out for. It's all very well participating taking the medications, but if you don't know what to look for in terms of some improvement, how can you assess at least if it was successful? **(Service User)**

This scepticism about the prevailing focus on biomedical causes of mental health presents a challenge for stratified medicine which takes the biomedical model as its starting point. As one services user advocated in the focus groups there is support for consideration of non-biomedical causes and, consequently, treatment, of psychosis.

But it seems to be all the same route of the sort of chemical imbalance. I did get invited to a lecture here actually, about the social origin of psychosis and I've heard [from] a lot of people with a diagnosis that it's created sometimes by a traumatic experience. Is the manifestation of psychosis really to do with chemicals at all? **(Service User)**

These concerns were echoed by some participants in the public dialogue, a number of whom felt that a stratified approach would lead healthcare professionals to focus on screening and testing protocols rather than a holistic assessment of the individual based on face to face interaction and knowledge of their situation. They were concerned for patients' emotional needs to be taken into account alongside their medical needs.

> Rather than looking at the whole person you could end up looking at patients on the basis of a load of stats. **(Dialogue participant, London public group)**

Acceptability of diagnostic tests

Both the public dialogue and the service user/carer research asked participants to consider different types of diagnostic tests which could be used in a stratified system to identify likely treatment response. Understanding which tests are acceptable to patients should be important to those developing new approaches, as it will influence adherence and outcomes. At the outset, the researchers assumed that the physical invasiveness of tests would be the primary factor in determining their acceptability to patients. However, for all groups, the emergent picture was more complicated. Alongside physical invasiveness, there were concerns about subjective tests which involve some aspect of judgement from medical professionals and where the data collected were seen as personal. We can hypothesise two dimensions of concern about testing – one based on the physical experience of the test itself (what we typically call ***invasiveness***). The other, which we might call ***intrusiveness,*** is based on the type of data collected and the potential for negative social consequences to arise from use and misuse of those data.

Crucially, the carer group disagreed with the 'hierarchy of invasiveness' suggested by the academic researcher, in which neuropsychological tests would be the least invasive form of assessment. In fact, the carers believed these would be very invasive on two grounds: first, they would require sustained concentration over a long period of time which they felt their relatives would find difficult and tiring. Secondly, the carer group thought that 'testing' for attributes such as intelligence and cognitive functioning and would provoke anxiety and a feeling of being judged. Blood tests, conversely, they regarded as completely routine and without problems. For the service user groups the picture was not so straightforward: most thought blood tests acceptable, though some people described a fear of needles. . There was no clear view on neuropsychological tests, although concerns were voiced that puzzles could be "quite confusing and difficult" (Service user).

For the public, lifestyle questionnaires and psychological interviews were particular examples of testing seen as intrusive, with participants describing these as more 'personal' than physical investigations. When probed on this, participants feared data being 'used against you' – perhaps indicating a lack of trust in the outcomes of subjective testing. When asked specifically about testing in a mental health context, even for physical tests, public participants were more concerned with confidentiality and data privacy than for physical conditions, with the exception of sexually transmitted diseases. A related tendency was for participants to be more concerned about genetic testing than other procedures; the public were very sensitive to the idea that genetic testing could reveal the potential for disease in the future, which would have immediate implications for insurance or employment. In both cases, the public were concerned not just with the procedure of the test but the type of data it produced suggesting that the acceptability of a testing protocol could decrease if the data produced were more 'personal'. It seems that invasiveness alone is not a good predictor for the acceptability of a test.

Among tests regarded as physically invasive, there was a sense of hierarchy from service user participants, which did accord with the researcher's expectations. The longer and more

complex the procedure, the more anxious participants were about taking part. Many participants, or their relatives, had actually already undergone MRI scans and at this point in the focus group discussions, there was varied willingness to have a similar MRS scan to establish neurochemical pathways and guide pharmacological intervention.

> But I wouldn't mind having a brain scan, something like that, just to have a look at say the chemical reactions in the brain. See I've had one of those scans before. **(Service User)**

> I've had all sorts of tests, I've been scanned in all different ways and I thought it'd be just like everything else, piece of cake. That's the only thing I've not been able to do. They can stick needles in me all over, it doesn't bother me in, in any way or they can operate on me, I'd rather see what's going on. I had a...knee replaced under an epidural and that was most interesting but could I go IN there! **(Service User)**

Again participants talked about side effects, and in particular the way they might affect a service user's ability to undergo a diagnostic test, regardless of their willingness to do so:

> Yes. Also if you've had Clozapine and you put on a lot of weight. **(Carer 1)** Chances of you getting in the tube... **(Carer 2)**

For more involved procedures such as PET scans (which involve drip infusions and chemical tracers and last for two to three hours) most participants viewed the tests as a "last resort" and "too much hard work". Again the side effects of medication came up, with one carer suggesting her daughter:

> Certainly would need to go to the loo many times with the incontinence thing, but ... I don't know that she would sit that long (Carer)

Despite these concerns participants across the public and service user groups tended to take a pragmatic view that even unpleasant or undesirable tests could be acceptable if they might significantly improve the process of finding a successful treatment:

> It's got to be better than going through changing tablets after tablets and them not working, you know what I mean and .... Your life, you know what I mean? These tests at the end of the day, you know at least you get an answer. **(Service User)**

Participating in research

Researchers hope that by looking at the treatment responses of a large enough number of patients, it will be possible to identify factors which predict that response. For example, Cancer Research UK is currently collecting tumour samples from up to 9000 cancer patients to produce a database for researchers to develop stratified and targeted treatments. The public dialogue found that people are generally agreeable to contributing to medical research – e.g. through trial participation or sharing medical records - strongly supporting the idea that they could contribute to improved outcomes for future patients.

This was echoed in the service user research where many of the participants who had misgivings about MRS and PET in a clinical context nonetheless said they would be willing to participate in a trial. Some thought that this might help them personally, but most understood that it would not; that their involvement could instead benefit future patients and service users.

> But if [name] consented to it, if she knew what was going to go on and she consented to it...I think she would want to help because she would feel that she was helping other people by doing this **(Carer)**

Despite this general support, the public, patients and carers all identified concerns about how this research might take place. For the public, most concerns were around the uses to which medical data are put; they had strong views on the rights of private companies to benefit commercially from research which they entered into from altruistic motives. For carers of service users, the most pressing concern was whether participating in any kind of trial would lead to deterioration in the condition of someone who was responding well to their current drug treatment. In one case, a carer held to this view even when one participant pointed out that for those who were stable on dopaminergic drugs, there would be no change in medication, merely a confirmation.

Consent was another issue raised frequently: for example, public participants, when asked specifically about the participation of mental health service users in research, were primarily concerned with the capacity of patients to consent to take part in trials. Among service users, an issue that preoccupied the participants was getting enough information:

> Yeah I would but it just depends on what kind of study it was. If the doctor explained it all first. And if I didn't feel as though I was ready for that study, I wouldn't do it. **(Service User)**

This was repeated in the public dialogue, where participants felt strongly that they would only take part in research where consent was truly informed. For the public, this meant understanding who would have access to the data collected, the security and governance arrangements, and the purpose of the research. Alongside the desire for research to be carried out in such a way as to minimise the possibility of abuse, participants also felt there

was value in the consent process, as recognition of the active contribution of research participants:

> This has to be an informed choice; they have to have the respect to ask **(Dialogue participant, Glasgow public group)**

Discussion

These two research projects demonstrate that there is a good baseline of support for approaches which minimise trial and error by identifying biomarkers for likely treatment response. This is especially true in areas like psychiatry where drug side effects can be severe. However, this is not to say that there is universal agreement on a definition of stratified medicine, or on how this type of approach should develop, and fundamental questions remain about the wisdom of focusing entirely on biomedical causes. The more practical concerns of research participants about taking different types of diagnostic test (whether physically invasive or personally intrusive) also have implications for adherence. Suggestions from public and service users were to have other patients with experience of an intervention who could talk through the procedure. These issues apply equally to the research context, where success in clinical trials relies on the participation of a robust sample of patients.

This type of social research early in the process of clinical research and policy development can offer valuable insights into the eventual consequences of the research/policy in question. In this case, SURE were also able to incorporate the service user voice – one which is still often marginalised. This ensures that new treatments are designed and evaluated from the ground up, with service users engaged throughout as informed collaborators rather than passive subjects.

About the authors

Diana Rose, PhD, Co-director and Jennifer Walke, Researcher, Service User Research Enterprise (SURE), Institute of Psychiatry, King's College London

The Service User Research Enterprise (SURE) undertakes research that tests the effectiveness of services and treatments from the perspective of people with mental health problems and their carers. SURE aims to involve service users in a collaborative way in the whole research process: from design to data collection, through to data analysis and dissemination of results.

Diane Beddoes, Chief Executive and Lucy Farrow, Project Manager, OPM Group

OPM is an independent, employee-owned research organisation and consultancy. We work with leaders, policymakers, regulators, commissioners and providers – as well as service users and communities – to ensure that services are designed and implemented efficiently, effectively and in the public interest.

The authors would like to thank James MacCabe for his help with this article.